

PRIORITY DOCUMENT

SUBMITTED OR TRANSMITTED IN
COMPLIANCE WITH RULE 17.1(a) OR (b)



The Patent Office
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

I also certify that the attached copy of the request for grant of a Patent (Form 1/77) bears an amendment, effected by this office, following a request by the applicant and agreed to by the Comptroller-General.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Signed

Anastasios

Dated 1 October 2004

BEST AVAILABLE COPY

28 OCT 03 EB47680-1 D02029
P01/7700 0.00-0325051.1

Patents Form 1/77

Patents Act 1977
(Rule 16)

27 OCT 2003

The
Patent

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

1/77

The Patent Office
Cardiff Road
Newport
Gwent NP9 1RH

MAR/KMM/PB60562P

1. Your reference

2. Patent application number

(The Patent Office will fill in his part)

0325051.1

3. Full name, address and postcode of the or of each applicant (*underline all surnames*)SmithKline Beecham Corporation
One Franklin Plaza, P.O. Box 7929, Philadelphia,
Pennsylvania 19101, United States of AmericaPatents ADP number (*if you know it*)

05949417004

United States of America

Pennsylvania

A/L 19/1/03
PPS.

4. Title of the invention

New Process

5. Name of your agent (*if you have one*)

Corporate Intellectual Property

"Address for service" in the United Kingdom
to which all correspondence should be sentGlaxoSmithKline
Corporate Intellectual Property (CN9 25.1)
980 Great West Road
BRENTFORD
Middlesex TW8 9GS

(including the postcode)

08072555006

Patents ADP number (*if you know it*)6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or each of these earlier applications and (*if you know it*) the or each application numberCountry Priority application number
(*if you know it*) Date of filing
(*day / month / year*)

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application Date of filing
(*day / month / year*)

8. Is a statement of inventorship and of right

BEST AVAILABLE COPY

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form.
Do not count copies of the same document

Continuation sheets of this form

Description	9
Claim(s)	2
Abstract	1
Drawings	NONE

JML

10. If you are also filing any of the following, state how many against each item.

Priority Documents

Translations of priority documents

Statement of inventorship and right to grant of a patent (*Patents Form 7/77*)

Request for preliminary examination and search (*Patents Form 9/77*)

Request for substantive examination
(*Patents Form 10/77*)

Any other documents
(please specify)

11.

We request the grant of a patent on the basis of this application

Signature *Michael Reed* Date 27-Oct-03
- M A Reed

12. Name and daytime telephone number of person to contact in the United Kingdom

M A Reed 020 80474455

Warning

After an application for a Patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 12 of the Patents Act 1977 stops you from applying for a patent abroad without first getting my written permission unless my application has been filed before the date of application in the United Kingdom. This means that you cannot apply for a patent in another country until my permission is granted. If you do apply for a patent abroad without my permission, I may be able to oppose the application in the United Kingdom.

BEST AVAILABLE COPY

attached to this form.
d) *If you have answered 'Yes' Patents Form 7/77 will need to be filed.*
f) *For details of the fee and ways to pay please contact the Patent Office.*

Patents Form 1/77

to grant of a patent required in support of
this request? (Answer yes if:

- a) any applicant named in part 3 is not an inventor, or
- b) there is an inventor who is named as an applicant, or
- c) any named applicant is a corporate body

See note (d)

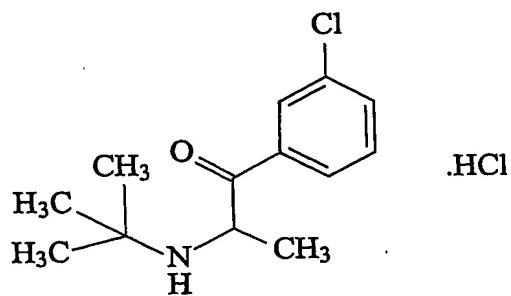
Yes.

NEW PROCESSBACKGROUND OF THE INVENTIONField of the Invention

5 The present invention relates to a process for making (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (hereinafter the "(2S, 3S) enantiomer") and pharmaceutically acceptable salts such as the hydrochloride salt of the (2S, 3S) enantiomer by dynamic kinetic resolution (DKR).

10 2. Description of the Prior Art

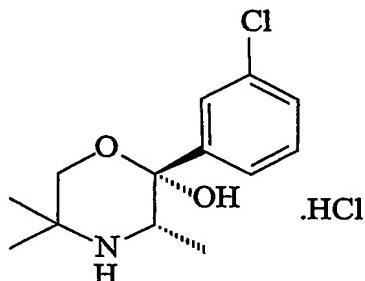
Bupropion hydrochloride, (\pm)-1-(3-chlorophenyl)-2-[(1,1-dimethyl-ethyl)-amino]-1-propanone hydrochloride, shown below, is the active ingredient of Wellbutrin[®] which is marketed in the United States for the treatment of depression. It is also the active ingredient of Zyban[®] which is marketed in the United States as an aid to smoking cessation. Bupropion is a 15 relatively weak inhibitor of the neuronal uptake of noradrenaline (NA), serotonin and dopamine (DA), and does not inhibit monoamine oxidase. While the mechanism of action of bupropion, as with other antidepressants, is unknown, it is presumed that this action is mediated by noradrenergic and/or dopaminergic mechanisms. Available evidence suggests that Wellbutrin[®] is a selective inhibitor of noradrenaline (NA) at doses that are predictive of antidepressant activity 20 in animal models. (See Ascher, J. A., et al., Bupropion: A Review of its Mechanism of Antidepressant Activity. Journal of Clinical Psychiatry, 56: p. 395-401,1995.)



25 Bupropion is extensively metabolized in man as well as laboratory animals. Urinary and plasma metabolites include biotransformation products formed via hydroxylation of the tert-butyl group

and/or reduction of the carbonyl group of bupropion. Four basic metabolites have been identified. They are the erythro- and threo-amino alcohols of bupropion, the erythro-amino diol of bupropion, and a morpholinol metabolite. These metabolites of bupropion are pharmacologically active, but their potency and toxicity relative to bupropion have not been fully characterized. Because the plasma concentrations of the metabolites are higher than those of bupropion, they may be of clinical importance.

The (2S, 3S) enantiomer of the morpholinol metabolite (2R*, 3R*) racemate has been found to be an active metabolite, and the hydrochloride salt of this enantiomer, as shown below, is a preferred salt.



10

The (2S,3S) enantiomer and pharmaceutically acceptable salts and solvates thereof, and pharmaceutical compositions comprising the same are useful in treating numerous diseases or disorders such as depression, attention deficit hyperactivity disorder (ADHD), obesity, migraine, pain, sexual dysfunction, Parkinson's disease, Alzheimer's disease, or addiction to cocaine, alcohol or nicotine-containing (including tobacco) products. For instance, reference is made to co-pending U.S. Application Serial No. 10/150,287, U.S. Patent No. 6,342,496 B1, issued to Jerussi et al. on January 29, 2002, U.S. Patent No. 6,337,328 B1, issued to Fang et al. on January 8, 2002, U.S. Patent Application Publication Nos. 2002/0052340 A1, 2002/0052341 A1, and 2003/0027827 A1 as well as WO 01/62257 A2. The methods of treating these diseases and disorders as described in these references and the references cited therein are herein incorporated by reference.

The references cited in the preceding paragraph describe and exemplify the claimed invention.

10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320 330 340 350 360 370 380 390 400 410 420 430 440 450 460 470 480 490 500 510 520 530 540 550 560 570 580 590 600 610 620 630 640 650 660 670 680 690 700 710 720 730 740 750 760 770

racemate. However, the method described in each of these references differs from the present invention in both procedure and result. These references relate to chemical resolutions of the racemate, whereas the present invention involves DKR which results in the chemical conversion of the (2R, 3R) enantiomer to the (2S, 3S) enantiomer, so that the yields of the (2S, 3S) enantiomer are greater than 50% based on the concentration of the racemic mixture of the (2R, 3R) and (2S, 3S) enantiomers. In the simple chemical resolution of the racemate, these references must isolate the desired diastereomeric morpholinol from a mixture of diastereomeric salts. The maximum yield of the desired diastereomer can therefore be at most 50% based on the concentration of the mixture of the (2R, 3R) and (2S, 3S) enantiomers.

In general, most chemical or enzymatic resolutions of a racemic material produce the desired enantiomer or mirror image diastereoisomer in a maximum theoretical yield of 50%. The undesired enantiomer or mirror image diastereoisomer is discarded as waste. In rare cases, a DKR can be employed to give a maximum theoretical yield of 100% of a desired enantiomer via equilibration of the enantiomers during the resolution. However, DKR's are extremely rare for the preparation of single pure diastereoisomers (particularly, for example, compounds containing two chiral centers), since both chiral centers must be capable of equilibration.

SUMMARY OF THE INVENTION

Accordingly, it is an object of the present invention to provide a novel process for producing a salt of the (2S, 3S) enantiomer that is essentially enantiomerically pure from an initial sample comprising the (2R, 3R) enantiomer by DKR in a yield of greater than 50% based on the initial sample.

When the present invention is compared with prior methods of isolation, it will be apparent that according to the present invention, there will be a much higher yield of the target compound, the (2S, 3S) enantiomer, and the inactive (2R, 3R) enantiomer will be present in such low concentrations as to not seriously diminish the pharmaceutical effectiveness of the product.

In one embodiment, the present invention is drawn to a DKR process for preparing a salt of the (2S, 3S) enantiomer that comprises:

mixing i) a sample comprising the (2R, 3R) enantiomer, ii) at least one solvent having a boiling point of at least 50°C and iii) 1.1 equivalent or higher of (-)-(R, R)-di-p-toluoyl-L-tartaric acid (hereinafter "L-DTTA") in any order, heating the mixture to at least 50°C for at least 1 hour

to form crystals comprising the L-DTTA salt of the (2S, 3S) enantiomer, and isolating the crystals, wherein the yield of the L-DTTA salt of (2S, 3S) enantiomer is greater than 50% based on said sample.

5 **DETAILED DESCRIPTION OF THE INVENTION**

The present invention provides a method for making the (2S, 3S) enantiomer, a single diastereoisomer from a two-chiral center racemate. The process is an example of a crystallization-induced asymmetric transformation, also termed a second-order asymmetric transformation, but, importantly with two chiral centers equilibrating. (For one chiral center equilibrating asymmetric transformations see "Crystallization-Induced Asymmetric Transformations" in Jacques, J., Collet, A. and Wilen, S. H., in Enantiomers, Racemates and Resolutions, Krieger Publishing Company, Malabar, FL, 1991, Chapter 6, pp. 369-377). These processes are also referred to as DKR as disclosed in "Enantioselective Synthesis: The Optimum Solution", Partridge, J. J. and Bray, B. L. in Process Chemistry in the Pharmaceutical Industry, (Gadamasetti, K. G., Ed.) Marcel Dekker, New York, NY, 1999, pp. 314-315.

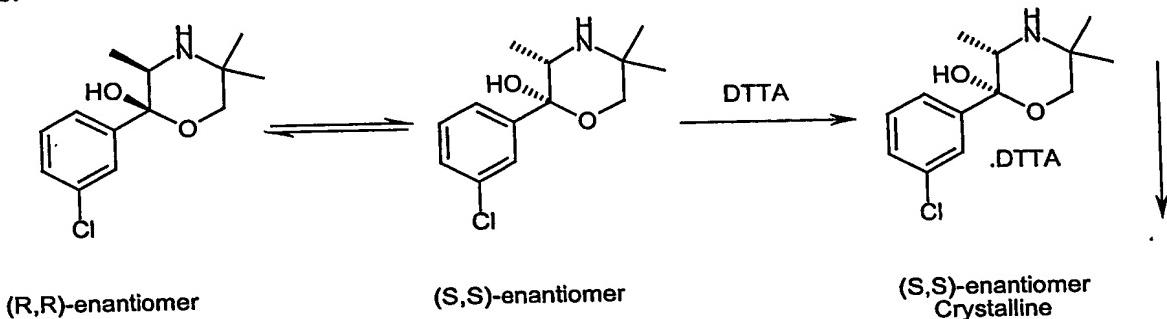
In one embodiment, the process for preparing a salt of the (2S, 3S) enantiomer comprises: mixing i) a sample comprising the (2R, 3R) enantiomer, ii) at least one solvent having a boiling point of at least 50°C and iii) 1.1 equivalent or higher of L-DTTA in any order, heating the mixture to at least 50°C for at least 1 hour to form crystals comprising the L-DTTA salt of the (2S, 3S) enantiomer, and isolating the crystals, wherein the yield of the L-DTTA salt of (2S, 3S) enantiomer is greater than 50% based on said sample.

The solvent for use in the inventive process can be any type, so long as the solvent will preferably dissolve the L-DTTA salt of the (2R, 3R) enantiomer over the L-DTTA salt of the (2S, 3S) enantiomer. Preferably the solvent has a boiling point of at least 50°C. More preferably, the solvent has a boiling point of 55-110 °C. Most preferably, the solvent is at least one selected from the following: alkyl acetate, such as methyl acetate, ethyl acetate (sometimes referred to herein as "EtOAc"), isopropyl acetate, propyl acetate, butyl acetate; dialkyl ketone such as 2, 4-

3R) and (2S, 3S) enantiomers) is 1.1 equivalents or higher. Preferably, the amount is 1.2-2.0 equivalents. More preferably, the amount is 1.3-1.5 equivalents.

In an embodiment of the invention, the crystallization of the target compound is promoted by adding a seed crystal of a salt of the (2S, 3S) enantiomer to said mixture.

The mixture of the sample comprising the (2R, 3R) enantiomer, solvent and L-DTTA is heated to at least 50°C. Preferably, the mixture is heated to reflux. While the mixture is being heated, the following equilibrium reaction between the (2R, 3R) and (2S, 3S) enantiomers proceeds:



By maintaining the mixture at a temperature of at least 50°C for a sufficient period of time, the crystallization of the L-DTTA salt of the (2S, 3S) enantiomer removes the (2S, 3S) enantiomer from the equilibrium thereby driving the equilibrium to the right (as shown above). Preferably, the mixture is heated for at least 1 hour. More preferably the mixture is heated for at least 5 hours. Most preferably, the mixture is heated for 10-16 hours.

As heating proceeds, the crystals of the L-DTTA salt of the (2S, 3S) enantiomer begin to form. These crystals may also contain the undesired (2R, 3R) enantiomer (as a salt) based on the type of solvent chosen for the DKR. In other words, the DTTA salt of the undesired (2R, 3R) enantiomer may be partially insoluble in the chosen solvent and a portion thereof crystallizes with the DTTA salt of the required (2S, 3S) enantiomer. However, the solvents of the present invention will have a much higher preference for dissolving the DTTA salt of the (2R, 3R) enantiomer thereby leading to a product having relatively high enantiomeric purity. In the present invention, the enantiomeric purity of the (2S, 3S) enantiomer in the crystals of the present invention is at least 80%. Preferably, the enantiomeric purity is at least 92%. More preferably, the enantiomeric purity is at least 96%. Most preferably, the enantiomeric purity is at least 98.5%. As used herein, an "essentially enantiomerically pure" sample, contains the (2S, 3S) enantiomer in at least 96%.

In an embodiment of the present invention, the process forms the L-DTTA salt of the (2S, 3S) enantiomer in a yield of at least 50% based on the initial sample comprising the (2R, 3R) enantiomer. Preferably, the yield is at least 60%. Most preferably, the yield is at least 75%.

In an embodiment of the present invention, the process further comprises a step of 5 converting the L-DTTA salt of the (2S, 3S) enantiomer to another salt. Preferably, said another salt is a pharmaceutically acceptable salt, such as a hydrochloride salt.

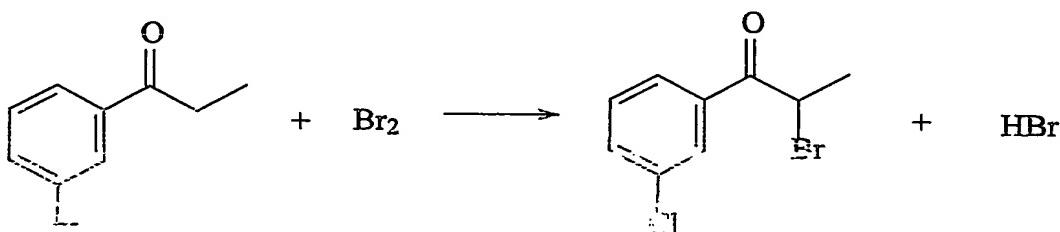
The method for preparing the racemate is not particularly limited. The methods described in U.S. Patent No. 6,342,496 B1, U.S. Patent No. 6,337,328 B1, U.S. Patent Application Publication Nos. 2002/0052340 A1, 2002/0052341 A1, and 2003/0027827 A1 as well as WO 10 01/62257 A2 are herein incorporated by reference. A particularly preferred method is now given; however, it should be understood that the specific examples, while indicating preferred embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

15

EXAMPLES

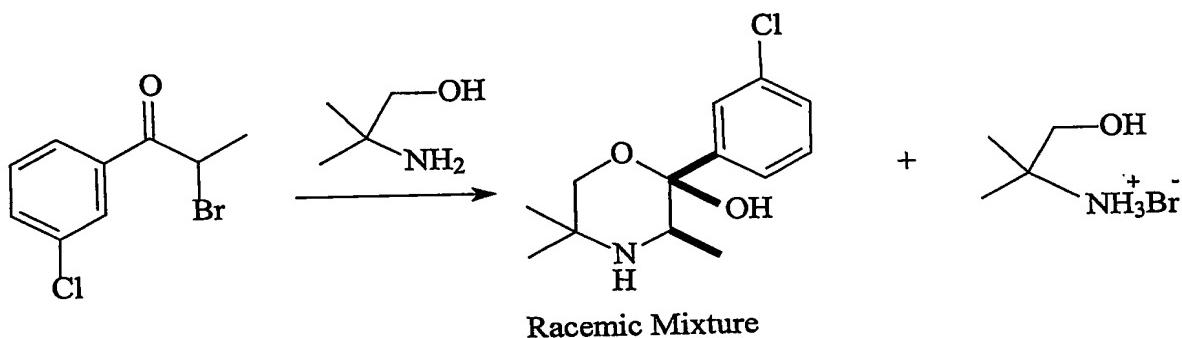
Synthesis of the Racemate:

3'-Chloropropiophenone (25g, 0.148mol) was gently stirred and heated to 50°C until 20 molten. Bromine (23.9g, 0.149mol, 1.01equiv.) was added, keeping the temperature at 50-55°C. The crude bromoketone was gently purged with nitrogen then heated at 75-80°C for 30 minutes to expel hydrogen bromide.



approximately 90°C, heating bath at 115°C), then 95% 2-amino-2-methylpropanol (34.7g containing 5% water, 0.37mol, 2.5 equivalents) was added slowly, while maintaining reflux. The mixture was then boiled under reflux for 3.0 hours. The hot mixture was diluted with water (30ml) then ethyl acetate (35ml), stirred for 5 minutes, then transferred to a separating funnel, washing with water (45ml) then ethyl acetate (65ml). The temperature of the mixture was maintained above 40°C during workup to minimize the risk of crystallization.

The organic phase was separated then washed with water (75ml). The solution containing the racemate was concentrated to approximately 64ml at atmospheric pressure then diluted with fresh ethyl acetate (86ml). Distillation was continued until a further 86ml of distillate was collected. The solution was diluted with ethyl acetate (107ml) then sampled for water determination. If the water content was greater than 0.1% a further 86ml of ethyl acetate was distilled out. The solution was then diluted to 300ml (275.8g) with ethyl acetate.



15

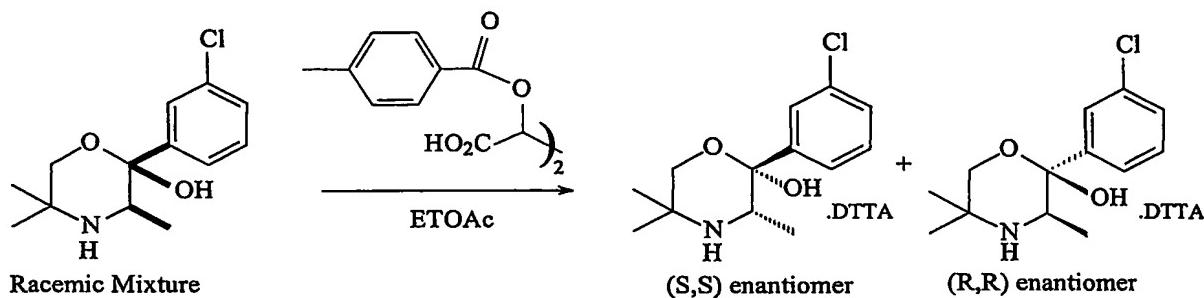
Synthesis of the target (2S, 3S) enantiomer

Example 1

A solution of L-DTTA (74.43g, 0.192mol, 1.3 equiv) in ethyl acetate (100ml) was prepared in a 1000ml flask and heated to reflux. 45 ml of the solution of racemate in ethyl acetate prepared above was added to the boiling L-DTTA as rapidly as possible. Without delay seed crystals of the L-DTTA salt of the (2S, 3S) enantiomer (0.05g) were added and boiling continued for about 1 hour. The remainder of the solution of racemate in ethyl acetate prepared above was added to the boiling L-DTTA solution over a period of 5 hours, and was rinsed with ethyl acetate (17.8ml). Reflux was continued for a further 14 hours. The suspension was cooled

to ambient temperature. The product was filtered off, washed with ethyl acetate (3x100ml, some of the wash can be used to wash out the vessel) then dried at 50°C under vacuum, to give 70.7g (74% yield based on the 3'-chloropropiophenone starting material) of the L-DTTA salt of the (2S, 3S) enantiomer as white crystals.

5



Example 2

(2R*, 3R*) racemate (a 50/50 mixture of the (2R, 3R) and (2S, 3S) enantiomers, 0.5g) 10 was dissolved in 5 mL of the solvent described in Table 1, below, then added to a stirred solution of L-DTTA (1.13 grams, 1.5 equiv) in 3 mL of the same solvent in a heating bath at 80°C. The mixture was stirred and heated for 18 hours, then cooled. The product was filtered off, washed with fresh solvent and dried to give product having the enantiomer ratio described in the following Table 1.

15

Table 1: Resolution of the (2R*, 3R*) racemate in various solvents.

Example	Solvent	Isomer Ratio 2S,3S : 2R,3R
2A	Methyl Acetate	99.6 : 0.4
2B	Isopropyl Acetate	99.8 : 0.2
2C	Propyl Acetate	99.6 : 0.4
2D	Isobutyl Acetate	98.6 : 1.4
2E	Butyl Acetate	99.0 : 1.0
2F	Ethyl Acetate	99.7 : 0.3
2G	2,4-Dimethyl-3-Pentanone	99.6 : 0.4
2H	3-Methyl-2-Butanone	99.8 : 0.2
2I	2-Butanone	99.9 : 0.1
2J	4-Methyl-2-Pentanone	99.7 : 0.3
2K	Acetonitrile	99.8 : 0.2
2L	Propionitrile	99.9 : 0.1
2M	Diethylene Glycol	99.9 : 0.1

Example 3

5 A sample of the (2R, 3R) enantiomer (0.5g) was dissolved in ethyl acetate (5ml) then added to a stirred boiling solution of L-DTTA (1.13g, 1.5equiv) in ethyl acetate (3ml). The mixture was heated at reflux for 18 hours then cooled. The product was filtered off, washed with ethyl acetate and dried to give a 70% yield of the L-DTTA salt of the (2S, 3S) enantiomer.

10 All cited patents, publications, co-pending applications, and provisional applications referred to in this application are herein incorporated by reference.

The invention being thus described, it will be obvious that the same may be varied in many ways. Such variations are not to be regarded as a departure from the spirit and scope of the present invention, and all such modifications as would be obvious to one skilled in the art are 15 intended to be included within the scope of the following claims.

CLAIMS

1. A process for preparing a salt of (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol that comprises:
mixing i) a sample comprising (-)-(2R, 3R)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol ((2R, 3R) enantiomer), ii) at least one solvent having a boiling point of at least 50°C and iii) 1.1 equivalent or higher of L-DTTA in any order, heating the mixture to at least 50°C for at least 1 hour to form crystals comprising an L-DTTA salt of (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol ((2S, 3S) enantiomer), and isolating the crystals, wherein the yield of the L-DTTA salt of the (2S, 3S) enantiomer is greater than 50% based on said sample.
2. The process according to claim 1, wherein the solvent preferably dissolves the L-DTTA salt of the (2R, 3R) enantiomer over the L-DTTA salt of the (2S, 3S) enantiomer.
3. The process according to claim 1 or claim 2, wherein the solvent is at least one selected from alkyl acetate, dialkyl ketone, nitrile, and a polyalcohol.
4. The process according to claim any one of claims 1 to 3, wherein the amount of L-DTTA is 1.2-2.0 equivalents.
5. The process according to any one of claims 1 to 4, wherein the mixture of the sample comprising the (2R, 3R) enantiomer, solvent and L-DTTA is heated to reflux.
6. The process according to any one of claims 1 to 5, wherein the mixture is heated for at least 5 hours.
7. The process according to any one of claims 1 to 6, wherein the crystals are essentially enantiomerically pure with respect to the (2S, 3S) enantiomer.
8. The process according to any one of claims 1 to 7, which is a continuous process.
9. The process according to any one of claims 1 to 8, wherein the sample comprising the (2R, 3R) enantiomer is a racemic mixture of the (2R, 3S) enantiomer and the (2S, 3R)

10. The process according to any one of claims 1 to 8, wherein the sample comprising the (2R, 3R) enantiomer is a non-racemic mixture of the (2R, 3R) enantiomer and the (2S, 3S) enantiomer.
11. The process according to any one of claims 1 to 8, wherein said sample comprising the (2R, 3R) enantiomer contains at least 50wt% of the (2R, 3R) enantiomer based on the weight of said sample.
12. The process according to any one of claims 1 to 8, wherein the sample comprising the (2R, 3R) enantiomer is essentially enantiomerically pure (2R, 3R) enantiomer.
13. The process according to any one of claims 1 to 12, wherein said sample comprising the (2R, 3R) enantiomer is formed in a step comprising reacting 2-bromo-3'-chloropropiophenone with 2-amino-2-methylpropanol.
14. The process according to any one of claims 1 to 13, further comprising a step of converting the L-DTTA salt of the (2S, 3S) enantiomer to another salt which is pharmaceutically acceptable.
15. The process according to claim 14, wherein the other salt is a hydrochloride salt.

ABSTRACT OF THE DISCLOSURE

Disclosed is a method for preparing (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol and pharmaceutically acceptable salts such as the (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol hydrochloride salt via dynamic kinetic resolution.

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- BLACK BORDERS**
 - IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
 - FADED TEXT OR DRAWING**
 - BLURRED OR ILLEGIBLE TEXT OR DRAWING**
 - SKEWED/SLANTED IMAGES**
 - COLOR OR BLACK AND WHITE PHOTOGRAPHS**
 - GRAY SCALE DOCUMENTS**
 - LINES OR MARKS ON ORIGINAL DOCUMENT**
 - REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
 - OTHER:** _____
-

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.